REMARKS

The Examiner has acknowledged receipt of all of the documents as of November 27, 2002. However, Applicant is unsure as to what extent the Examiner has reviewed the extensive Affidavits of Dr. Langer previously provided. Clearly, Dr. Langer has provided his expert opinion as evidence with respect to refuting the cited prior art and the rejections based thereon in the Examiner's prior position. Surprisingly, the Examiner has chosen to substantially ignore Dr. Langer's opinion and has created another combination which is effectively no better and in most cases worse than the prior combination of Duclos and Crisp.

Dr. Langer is a well respected professional with extensive credentials that are set out in his extensive CV attached to his Declarations. He holds the position of the Kenneth J. Gerermeshausen Professor of Chemical and Biomedical Engineering at the Massachusetts Institute of Technology. This title given to Dr. Langer is one of distinction amongst his colleagues. His expert opinion therefore is paramount in this case and should be beyond question.

For example the Examiner has stated in her additional comments that the Declarations discussed Applicant's claimed invention as containing sorbitol and cefuroxime axetil. This is clearly not the case. At no time in the first Affidavit of Dr. Langer was there any limitation of the excipient to sorbitol only, but only as an example. In the second Affidavit, Dr. Langer provided his laboratory results with respect to comparing Glaxo's preferred composition (as set out in it's product monograph) versus the actual preferred composition manufactured by Apotex, the licensee of the instant application (as set out in it's product monograph). When providing a direct comparison of the marketed Glaxo product with the marketed Apotex co-precipitate, clearly sorbitol and zinc chloride are present. Dr. Langer therefore was providing his comments with respect to the preferred marketed embodiment and not to all of the embodiments of the invention. The Examiner is requested to fully reconsider the Affidavits of Dr. Langer, both first and second, which are incorporated by reference in their entirety to this response.

With regard to the Examiner's double patenting rejection Applicant does not agree with the Examiner in respect of a Terminal Disclaimer being required, nonetheless Applicant attaches herewith a terminal disclaimer disclaiming the term of any patent which might issue from this application with regard to United States Patent No. 6,485,744 B1 which is

commonly owned. The double patenting rejection therefore is moot in view of this submission. The correct fee is also attached.

Claims 1 to 20 now stand rejected under 35 USC 103(a) as being unpatentable over U.S. Patent No. 4,865,851 to James *et al* in view of U.S. Patent No. 5,776,495 to Duclos *et al* herein referred to as James and Duclos respectively hereinafter.

Referring now to James et al, United States Patent No. 4,865,851 also owned by Glaxo similar to the prior patent to Crisp cited by the Examiner, namely United States Patent. No. 4,820,833. Crisp required a highly pure substantially amorphous form of cefuroxime axetil to be present in its product. Dr. Langer had already provided his opinion in this regard as to the deficiencies of Crisp with respect to Applicant's co-precipitate. James sets out in its teachings the problem being addressed in the prior art of cefuroxime axetil as having an extremely bitter taste, that is to say the granules that are formed by Crisp when placed in a formulation, that is the highly pure cefuroxime axetil in the amorphous form, in order to make it acceptable as a dose, that the product be coated. The bitter taste problem may be minimized by formulating the cefuroxime axetil as a lipid coated particle.

At column 2, line 3 it states that Glaxo had found that the extremely bitter taste of cefuroxime axetil may be masked by the application to the cefuroxime axetil particles of a lipid coating which is substantially insoluable in water. At line 52 the first statement of the invention is provided which states that the cefuroxime axetil in particulate form includes an integral coating of lipid or a mixture of lipids which serve to mask the bitter taste of the cefuroxime axetil. At column 3, line 3 the invention is described as either cefuroxime axetil in crystal form or in preferably amorphous form as taught in the priority British Specification 2,127,401 which is equivalent to United States Patent No. 4,562,181 of Crisp the parent of 4,820,833 and in the same patent family. The James patent continues stating that the cefuroxime axetil might be undercoated with a substance prior to the final film coating. The film coating may include a number of alternatives which are stated in the patent and at line 15 of column 4, wherein the amorphous cefuroxime axetil is prepared in the form of hollow micro spheres of a predetermined size by a spray drying method as described in the above-mentioned priority British Patent Specification. The coated particles of the invention are prepared by atomizing a dispersion of particulate cefuroxime axetil in a molten lipid and cooling the coated particles thereby obtained. A pneumatic nozzle atomizer fitted in a standard spray drying/chilling apparatus is of particular value in preparing these coated

granules. The molten dispersion of cefuroxime axetil will be supplied to the atomizer head at a temperature in the range of 60 to 80 degrees centigrade and preferably between 65 to 75 degrees centigrade. Clearly, this is a different temperature range than one would require for spray drying and clearly the two fluid internal or external mixing pneumatic nozzle atomizer provides different performance to a spray drying/chiller than one would utilize for a spray drying process.

Continuing with the James patent, the Examiner had pointed out that the use of sorbitol is described in the patent at column 5. Clearly, the use of sorbitol is defined in James only as a bulk sweetener, that is to say as a flavouring agent at line 53 of column 5, for example, mint flavours such as peppermint flavouring agents and bulk sweeteners such as sorbitol and sucrose or artificial sweeteners. At no time is there any discussion of the sorbitol being utilized as an excipient for co-precipitating with cefuroxime axetil. Clearly, the Examiner has misread the reference and is attempting to reconstruct Applicant's invention by 20/20 hindsight using his invention as a blueprint which is not permitted. The granules are provided for oral administration comprising lipid coated particles of cefuroxime axetil. These granules therefore are in a much more complicated form than the granules that might be prepared by Crisp. The James particles of cefuroxime axetil are coated and potentially undercoated following the preparation of the preferred highly pure amorphous form. At column 6, line 61, it states that the cefuroxime axetil used in the examples was a highly pure spray-dried amorphous material prepared and described in the priority British Specification above-mentioned.

Referring to Example 1, a dispersion of the amorphous cefuroxime axetil was prepared with stearic acid powder at a 150 grams to 850 grams respectively by melting the lipid and raising the temperature of the molten lipid to about 15 degrees centigrade above its melting point and then adding the cefuroxime axetil with mixing, that is to say, adding 150 grams into 850 grams of the stearic acid powder. This molten lipid was then fed into a spray drier/chiller which had been fit with the previously mentioned pneumatic atomizing nozzle for that purpose and such molten mixture was then atomized with an air temperature of 65 to 70 degrees centigrade and the product resulting was chilled using a stream of air fed into the spray chamber at ambient temperature so that the solidified product could be collected. The various examples also include such a similar procedure. At column 10 in the examples at line 2 it states that the cefuroxime axetil was coated with maltodextrin as sweetening agent and then was coated with the stearic acid, a product of the prior examples.

Therefore, clearly the granular product of James is much more complicated than the product of Crisp and respectfully the Examiner has taken one step backwards in attempting to prepare a 20/20 hindsight reconstruction of Applicant's invention by combining James with the teachings of Duclos, which will be discussed hereinafter. The problem being addressed by James is masking the bitter taste. This is substantiated throughout his entire disclosure. The assignee, Glaxo is fully aware of the problems of bitterness and therefore attempted to patent, in addition to the highly pure substantially amorphous patent of Crisp, the masking of the bitter taste by undercoating and coating. There is no other objective of James. The Examiner's conclusion that the composition of James may include pharmaceutically acceptable additives including sorbitol in fact is obviously correct. Sorbitol is added as a sweetener. At no time is the sorbitol added to a solvent mixture with the cefuroxime axetil in crystalline form and completely dissolved and subsequently spray-dried to create the co-precipitate. Sorbitol is the preferred excipient but Applicant in no way restricts its claim set to this preferred excipient only. The fact that sorbitol is a pharmaceutically acceptable additive is not convincing. Clearly it is utilized as a sweetener and as a bulking agent in an admixture but heretofore it has not been used in preparation of a co-precipitate in combination with an active, such as cefuroxime axetil, in the manner as set out in Applicant's disclosure. The Examiner has correctly concluded that James does not teach a co-precipitate. Clearly, James teaches masking bitter taste only. The granules identified in James could not be used to prepare a co-precipitate since they are coated with a lipid which would severely impede, the granules from dissolving, and the spray drying process.

Referring now to Duclos et al, United States Patent No. 5,776,495, hereinafter referred to as Duclos there is taught at column 2, line 18, the product of a solid dispersion of at least one therapeutic agent "in" a hydrophilic "carrier". The resulting co-precipitate therefore is prepared by evaporating the solvent to dryness to form the combination. It is clear however, in examining Duclos closely, that the hydrophilic "carrier" is in fact present as a much higher percentage by weight than the active. At line 34 of column 2 it is stated, that Duclos had prepared studies that had shown that the dissolution rate will be increased when an organic solvent also contained a surface active agent, for example a surfactant. This is clearly defined in the Affidavit of Dr. Langer with respect to his analysis of Duclos, namely that the percentage by weight of the active in the hydrophilic carrier is below 50% in a majority of times; in all but one occurrence whereat it is stated, at column 5, line 35 in the case of progesteronic derivates one may realize co-precipitates containing from 10 to 60 percent by

weight of the active ingredient. This is the largest percentage indicated in James, but the preferred amount is stated further on at 15 to 35 percent. It would be difficult to provide a carrier for the active at that level of 60%. The preferred formulation also substitutes in part a surfactant at a range of 5 to 20 percent and a preferred range of 1 to 10 percent for some of the carrier. The difference will be the hydrophilic carrier. Polysorbate 80 is the preferred surfactant. In the detailed description at column 6, line 50 it states that the physical mixtures containing 20, 30 and 50 percent weight by weight of the active progesterone has been prepared with polyvinyl pyrrolidone with an additional amount of polysorbate 80 which displaces some of the polyvinyl pyrrolidone at 1, 5 or 10 percent weight by weight basis. The resulting co-precipitate would include no more than 50% weight basis and typically much less than the detailed examples. This ratio is repeated over and over in the disclosure. Referring to specifically the tables 1, 2 and 3, it clearly seen that the highest ratio is approximately 50% of progesterone to polyvinyl pyrrolidone, which is the "carrier". This is further supported at column 17 wherein fenofibrate is discussed and the co-precipitate produced includes from 50 down to 10 percent by weight of fenofibrate. Applicant in its claim set as amended provides at least 75% active, and it may therefore be properly concluded that the active might be correctly defined as the carrier.

Applicant has however prepared a co-precipitate that includes in its preferred examples, from 75% to 95% and preferably 90% cefuroxime axetil with the balance being an excipient. At no time therefore is the cefuroxime axetil carried in a hydrophilic carrier as part of the solid dispersion making up the co-precipitate of Applicant. This is an important distinction of Dr. Langer, in his second Affidavit which was previously provided and the contents of which with respect to the difference discussed above is hereby incorporated by reference in its entirety. Applicant in comparison to Duclos utilizes a minimum amount of excipient and yet provides a composition with acceptable dissolution properties. These properties by design reflect the tendency of cefuroxime axetil to gel in the gut if immediately disintegrated, and as set out again in Dr. Langer's first Affidavit, this would tend to interfere with the transport mechanism for cefuroxime axetil. Applicant therefore has designed its product to disintegrate and dissolve for example as indicated in Claim 1 and 3 set out below.

> 1. An enhanced bioavailable composition comprising a co-precipitate of cefuroxime axetil and a water-soluble excipient made by dissolving **about 10 parts by weight pure crystalline cefuroxime axetil and about 1 part by weight of the excipient** in a suitable solvent, and recovering the co-precipitate, said composition having a disintegration time of at least 10 to 30 minutes and having a dissolution as determined by U.S.

Pharmacopoeia 23rd Edition, of about 65% to about 80% in 20 minutes and about 80% to over 90% in 60 minutes.

3. An enhanced bioavailable composition comprising a co-precipitate of cefuroxime axetil and a water-soluble excipient made by dissolving **about 75% to about 95% by weight pure crystalline cefuroxime axetil and from about 5% to about 25% by weight water-soluble excipient** in a suitable solvent, and recovering the co-precipitate, said composition having a disintegration time of at least 10 to 30 minutes and having a dissolution as determined by U.S. Pharmacopoeia 23rd Edition, of about 65% to about 80% in 20 minutes and about 80% to over 90% in 60 minutes.

Applicant therefore has provided an unique composition of cefuroxime axetil with acceptable disintegration and dissolution properties which avoids saturating the transport mechanism and thereby prevents the gelling of the cefuroxime axetil when being ingested, as is the case with immediate disintegration as identified in the James and Crisp patents.

Another point which Applicant wishes to stress is that the active identified in Duclos is in fact cefuroxime which is an injectable active. There is no discussion of the esters of cefuroxime and in particular cefuroxime axetil. Glaxo has done quite a bit of research in this area and has provided various forms of cefuroxime including multiple esters as found in it's prior patents and the lysine salts thereof. Had Duclos intended that cefuroxime be listed as including its esters it would have done so since at column 4, line 3 it is indicated that estradiol and its esters is considered to be part of the relevant actives. Clearly, there was no intention that cefuroxime and its esters would be considered relevant since there is clearly no mention or discussion of cefuroxime in any respect in the patent other than as previously indicated a listing amongst other hardly water soluable active ingredients.

The Examiner has stated that Duclos teaches a process for the production of a solid dispersion of at least one therapeutic agent in a carrier. Applicant however does not include a co-precipitate as a solid dispersion of the therapeutic agent in a carrier. The Examiner respectfully is attempting a 20/20 hindsight reconstruction in a reading of Duclos in that she is not reading the detailed construction of Duclos, **namely that it is a solid dispersion of an active in a carrier**. Applicant provides no such composition. This is clearly supported in Applicant's comments above. Not only does Duclos not teach Applicant's dissolution times, but it clearly does not teach a minority of the water soluable excipient as set out with Applicant's composition. The preferred composition includes 90% cefuroxime axetil, 9% sorbitol, and 1% zinc chloride (from the Product Monograph). Therefore, the co-precipitate resulting from such a ratio cannot be considered to be an active in a hydrophilic carrier. In

fact, it is probably more appropriate to consider the composition as a hydrophilic excipient in an active also acting as the carrier.

How then can any combination of James in view of Duclos result in Applicant's specific combination as set out in Claims 1, 3 and 15 set out below.

> 1. An enhanced bioavailable composition comprising a co-precipitate of cefuroxime axetil and a water-soluble excipient made by dissolving **about 10 parts by weight pure crystalline cefuroxime axetil and about 1 part by weight of the excipient** in a suitable solvent, and recovering the co-precipitate, said composition having a disintegration time of at least 10 to 30 minutes and having a dissolution as determined by U.S. Pharmacopoeia 23rd Edition, of about 65% to about 80% in 20 minutes and about 80% to over 90% in 60 minutes.
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> 3. An enhanced bioavailable composition comprising a co-precipitate of cefuroxime axetil and a water-soluble excipient made by dissolving **about 75% to about 95% by weight pure crystalline cefuroxime axetil and from about 5% to about 25% by weight water-soluble excipient** in a suitable solvent, and recovering the co-precipitate, said composition having a disintegration time of at least 10 to 30 minutes and having a dissolution as determined by U.S. Pharmacopoeia 23rd Edition, of about 65% to about 80% in 20 minutes and about 80% to over 90% in 60 minutes.
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> 15. An enhanced bioavailable composition comprising a co-precipitate of cefuroxime axetil and sorbitol made by dissolving **about 10 parts by weight pure crystalline cefuroxime axetil about 1 part by weight of and the sorbitol** in a suitable solvent, and recovering the co-precipitate, said composition having a disintegration time of at least 10 to 30 minutes and having a dissolution as determined by U.S. Pharmacopoeia 23rd Edition, of about 65% to about 80% in 20 minutes and about 80% to over 90% in 60 minutes.

Referring to the traditional test enunciated in Graham vs. John Deere Company 383 U.S. 1, 148 U.S.P.Q. 459 1966, for Section 103 nonobviousness requires the fact finder to make several determinations. Applying the test to the case at hand the scope and content of both James and Duclos has been determined, the differences between the prior art and the claims at issue has been ascertained. The patentability of the claims at hand stems from the fact that the specific combination of the claimed elements set out in the independent claims 1, 3, and 15 and the claims depending thereupon was not disclosed in the prior art and the additional allegation that the specific combination of claimed elements set out in these claims is nonobvious to one of ordinary skill in the art.

It is well settled that obviousness under § 103 can not be established by combining the teachings of the prior art to obtain the claimed invention, absent some teachings, suggestion, or incentive supporting the combination from in this case James and/or Duclos. See In Re: Geiger, 2 USPQ 2d 1276 (Fed. Cir. 1987). By the same token, the Examiner can not pick and chose among the individual elements of James and/or Duclos, to recreate the claimed invention as set out in claims 1, 3, and 15. To the contrary, the Examiner has the burden to show some teachings or suggestion in James and/or Duclos to support the particular claimed combination. See Smithkline Diagnostics Inc. vs. Helena Laboratories Corp., 8 USPQ 2d 1468 (Fed. Cir. 1988).

Al-Site Corp. v. VSI Int'l, Inc., 50 USPQ 2d 1161, 1171 (Fed. Cir. 1999)

VSI is unable, however, to point to any specific teaching or suggestion for making this combination. VSI instead relies on what it presumes is the level of knowledge of one of ordinary skill in the art at the time of the invention to supply the missing suggestion to combine. In the first place, the level of skill in the art is a prism or lens through which a judge or jury views the prior art and the claimed invention. This reference point prevents these deciders from using their own insight or, worse yet, hindsight, to gauge obviousness. **Rarely, however, will the skill in the art component operate to supply missing knowledge or prior art to reach an obviousness judgment. . .. Skill in the art does not act as a bridge over gaps in substantive presentation of an obviousness case** (emphasis added), but instead supplies the primary guarantee of objectivity in the process.

The Examiner has stated that it is her position that the times of dissolution are a property of the formulation but the Examiner has not been able to prepare a combination which would result in rendering Applicant's formulation set out in claims 1, 3 and 15 as obvious. At best, the combination of James in view of Duclos results in a coated and potentially undercoated particle of cefuroxime axetil being utilized allegedly to prepare a solid dispersion in a hydrophilic carrier. Respectfully, the coated particles would not be suitable for preparing such a solid dispersion with Duclos and therefore clearly the teachings are **mutually exclusive**. If the lipid coating is placed in the solvent of Duclos it would remove at least some of the coating from the particles of cefuroxime axetil thereby rendering the effort to mask the bitter taste of cefuroxime axetil as being at least in part destroyed. No discussion of such a result is present in the Examiner's arguments since the Examiner did not thoroughly review the teachings of Duclos as Applicant has provided at this point in time. **Clearly therefore James and Duclos are not combinable**. There is no motivation within James to refer to Duclos since the problem being addressed in James is not the problem being addressed in Duclos. The two problems are mutually exclusive. Therefore, how can James in view of Duclos suggest a co-precipitate of cefuroxime axetil as set out in Applicant's amended claims when in fact there is no motivation in James to prepare a co-precipitate but to mask the bitter taste of the preferred form as prepared by British Patent Specification 2,127,401 relating to the highly pure substantially amorphous form of spray dried of cefuroxime axetil. If a co-precipitate were prepared utilizing the granules of James, when placed in solvent the lipid coating would dissolve and leave a grease film on the surface which would more than likely effect the alleged co-precipitate so prepared.

There is clearly no motivation to combine the teachings of James and Duclos since the teachings thereof are mutually exclusive. James may teach mixing cefuroxime axetil in its

highly pure substantially amorphous form as an admixture with common excipients such as sorbitol but clearly not for the purpose of preparation of a solid dispersion co-precipitate. Duclos generally teaches co-precipitates but only as solid dispersions of an active in a hydrophilic carrier. In fact, Duclos teaches the addition of a surfactant in order to enhance the dissolution of the resulting composition which is contrary to the direction Applicant wishes to take with its co-precipitate. Duclos did not even appreciate the problems identified with cefuroxime axetil gelling in the gut upon immediate dissolution and the desirability of delaying such a dissolution, for example by the means discussed by Applicant in its description and disclosure, in order to avoid the saturation of the transport mechanism in the gut utilized for the cefuroxime axetil. Clearly, there is no expectation of success therefore from any combination of James and Duclos, assuming that the Examiner's allegations that they can be readily combined is true which Applicant refutes in its entirety. Cleary, there is no discussion of making Applicant's co-precipitate including a majority of cefuroxime axetil and a minority of the excipient even though Duclos *et al* does discuss solid dispersions and co-precipitates, they specifically refer to the therapeutic agent being dispersed in a hydrophilic carrier. This is clearly set out above in Applicant's response and the Examiner cannot deny the facts regarding the Duclos disclosure.

In fact it is well established that for a combination of references to render an invention obvious, it must be obvious that the references can be combined; In Re Avery 186 U.S.P.Q.161 (CCPA 1975). The references themselves and not in retrospect, must suggest what has to be done. In Re: Skoll 187 USPQ 481 (CCPA 1975). There must be some reason for the combination other than hindsight gleaned from their invention itself. Interconnect Planning Corp., vs. Feil, 774 F. 2d 1132, 1134 (Fed. Cir. 1985). See also Panduit Corp. vs. Dennision Mfg. & Co., 810 F. 2d 1561, 1568 (Fed. Cir. 1988) where the court said:

> "Elements of separate prior art patents cannot be combined when there is no suggestion of such combination anywhere in those patents".

Although the Examiner suggests that the structure could readily be modified to form a combination of the claims at issue, the mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification. Please See in Re: Gordon 733 F. 2d 900-902, 221 USPQ 1125, 1127 (Fed. Cir. 1984); In Re: Grabiak, 769 F. 2d 729, 731, 226 USPQ 870, 872 (Fed. Cir. 1985).

Clearly, neither James nor Duclos suggests or provides any reason or motivation to make such a modification as purported by the Examiner. With reference to In Re: Regal, 526 F. 2d 1399, 1403 n. 6, 188 USPQ 136, 139 n. 6 (CCPA 1975).

> "There must be some logical reason apparent from positive, concrete evidence of record which justifies a combination of primary and secondary references".

In Re: Geiger, 815 F. 2d 686, 688, 2 USPQ 2d 1276, 1278 (Fed. Cir. 1987) (obviousness can not be established by combining pieces of prior art absence some "teachings, suggestion, or incentive supporting the combination"): In Re: Cho. 813 F. 2d 378, 382, 1 USPQ 2d 1662, 1664 (Fed. Cir. 1987)("discussing the Board's holding that the artisan would have been motivated to combine the references").

Therefore, it is Applicant's view there is no evidence of motivation in James and/or Duclos, either within the references themselves, or knowledge generally available to one of ordinary skill in the art, to make the purported changes suggested by the Examiner to arrive at the claimed subject matter.

Respectfully, the Examiner is creating a 20/20 hindsight reconstruction using Applicant's invention as a blue print to allegedly find elements of Applicant's combination in the prior art. This is not permissible as set out below.

In re Oetiker, 24 USPQ 2d 1443, 1446 (Fed. Cir. 1992)

> The combination of elements from non-analogous sources, in a manner that reconstructs the applicant's invention only with the benefit of hindsight, is insufficient to present a prima facie case of obviousness. **There must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the field of the invention would make the combination.** (emphasis added)That knowledge can not come from the applicant's invention itself.

ATD Corporation v. Lydall, Inc., 48 USPQ 2d 1321, 1329 (Fed. Cir. 1998)

> Determination of obviousness can not be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention. **There must be a teaching or suggestion within the prior art, or within the general knowledge of a person of ordinary skill in the field of the invention, to look to particular sources of information, to select particular elements, and to combine them in the way they were combined by the inventor.(emphasis added)**

In Re: Fritch, 23 U.S.P.Q. 2d 1780 (Fed. Cir. 1992)

> "Wilson and Hendrix fail to suggest any motivation for, or desirability of, the changes espoused by the Examiner and endorsed by the Board. Here, the Examiner relied upon hindsight to arrive at the determination of obviousness. **It is impermissible to use the claimed invention as an instruction manual or "template" to piece together the teachings of the prior art so that the claimed invention is rendered obvious**(emphasis added). The court has previously stated that "[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention."

In Re: Rouffet, 47 U.S.P.Q. 2d 1453 (Fed. Cir. 1998)

> *"As this court has stated, "virtually all [inventions] are combinations of old elements." Environmental Designs, Ltd. v. Union Oil Co., 713 F.2d 693, 698, 218 USPQ 865, 870 (Fed. Cir. 1983); see also Richdel, Inc. v. Sunspool Corp., 714 F.2d 1573, 1579-80, 219 USPQ 8, 12 (Fed. Cir. 1983) ("Most, if not all, inventions are*

combinations and mostly of old elements."). Therefore an examiner may often find every element of a claimed invention in the prior art. If identification of each claimed element in the prior art were sufficient to negate patentability, very few patents would ever issue. Furthermore, rejecting patents solely by finding prior art corollaries for the claimed elements would permit an examiner to use the claimed invention itself as a blueprint for piecing together elements in the prior art to defeat the patentability of the claimed invention. Such an approach would be "an illogical and inappropriate process by which to determine patentability." Sensonics, Inc. v. Aerosonic Corp., 81 F.3d 1566, 1570, 38 USPQ 2d 1551, 1554 (Fed. Cir. 1996).

To prevent the use of hindsight based on the invention to defeat patentability of the invention, ***this court requires the examiner to show a motivation to combine the references that create the case of obviousness. In other words, the examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.*** (emphasis added)

This court has identified three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art. In this case, the Board relied upon none of these. Rather, just as it relied on this high level of skill in the art to overcome the differences between the claimed invention and the selected elements in the references, it relied upon the high level of skill in the art to provide the necessary motivation. The Board did not, however, explain what specific understanding or technological principle within the knowledge of one of ordinary skill in the art would have suggested the combination. Instead, the Board merely invoked the high level of skill in the field of art. If such a rote invocation could suffice to supply a motivation to combine, the more sophisticated scientific fields would rarely, if ever, experience a patentable technical advance. Instead, in complex scientific fields, the Board could routinely identify the prior art elements in an application, invoke the lofty level of skill, and rest its case for rejection. To counter this potential weakness in the obviousness construct, the suggestion to combine requirement stands as a critical safeguard against hindsight analysis and rote application of the legal test for obviousness.

Because the Board did not explain the specific understanding or principle within the knowledge of a skilled artisan that would motivate one with no knowledge of Rouffet's invention to make the combination, ***this court infers that the examiner selected these references with the assistance of hindsight. This court forbids the use of hindsight in the selection of references that comprise the case of obviousness.*** (emphasis added)*See In re Gorman, 933 F.2d 982, 986, 18 USPQ 2d 1885, 1888 (Fed. Cir. 1991). Lacking a motivation to combine references, the Board did not show a proper prima facie case of obviousness. This court reverses the rejection over the combination of King, Rosen and Ruddy."*

Applicant therefore refutes the Examiner's conclusion that the claims contained herein are prima fascia obvious and full reconsideration is therefore requested.

With regard to the Examiner's additional comments, Applicant is well aware that independent claim 1 requires only cefuroxime axetil and a generic excipient. This is well supported by the evidence before the Examiner. The second Affidavit of Dr. Langer which compares the marketed products of Glaxo and Apotex, was provided as evidence of the differences with respect to the preferred embodiments of the invention, and specifically claim 15, in relation to the Glaxo product. If Applicant's invention is so obvious then why did not a renowned company such as Glaxo with all of its worldwide research activity and having experienced the problems associated with the gelling in the gut as set out in James at column 1, lines 55 to 60, arrive at Applicant's co-precipitate. This is clearly set out again in the first Affidavit of Dr. Langer to which the Examiner is referred for full reconsideration of the issues herein.

Applicant therefore has addressed each and every one of the issues of the Examiner and has refuted in its entirety the Examiner's alleged obviousness rejection of James in view of Duclos. This is simply not the case for the detailed reasons set out above and full reconsideration is respectfully requested, especially in view of Applicant's further amendments to independent claims 1, 3 and 15.

In view of the above amendments, Applicant respectfully submits that all pending claims are clearly allowable over the prior art James *et al* in view of Duclos *et al*. A full supervisory review is hereby requested should the Examiner find otherwise, that is a review by Examiner Thurman Page.

If the Examiner has any questions, she is respectfully requested to contact Applicants' Agent, Neil H. Hughes at (905) 771-6414 at her convenience.

Respectfully submitted,

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Agent for the Applicant

NHH:mse
Enclosures